Abstract P124 Table 1 Endpoint results

	UMEC + ICS/LABA N=119)	PBO + ICS/LABA (N=117)	Treatment Diff. vs PBO (95% CI)
Trough FEV1 at Day 85	n = 109	n = 110	
LS mean change from baseline, L (SE)	0.090 (0.0183)	-0.033 (0.0184)	0.123[a] (0.071, 0.174)
0–6 hours weighted mean FEV1 at Day 84	n = 107	n = 110	
LS mean change from baseline, L (SE)	0.184 (0.0176)	0.035 (0.0175)	0.148[a] (0.099, 0.197)
Rescue use (mean puffs/day)*	n = 119	n = 116	
LS mean change from baseline (SE)	-0.53 (0.105)	-0.15 (0.106)	-0.38[b] (-0.67, -0.10)
Rescue use (% rescue-free days)*,**	n = 119	n = 116	
Median (range)	76.8(0, 100)	62.9(0, 100)	0[c] (0.0, 3.4)
CAT score at Day 84	n = 110	n = 110	
LS mean change from baseline (SE)	-0.37 (0.457)	0.94 (0.457)	-1.31[b] (-2.59, -0.04)
TDI score at Day 84	n = 105	n = 109	
LS mean (SE)	1.07 (0.197)	0.67 (0.195)	0.40 (-0.15, 0.95)

[a]p<0.001; [b]p<0.05; [c]p = 0.640, non-parametric analysis; *use over 1–12 weeks; **non-parametric analysis of % rescue-free days was a post hoc analysis and replaced the pre-specified analysis (percentage rescue-free day datadid not satisfy normality assumptions for MMRM analysis); improvements in CAT scores are shown by negative changes.

Conclusions UMEC+ICS/LABA improved lung function and reduced rescue medication use (mean puffs/day) and CAT score in patients with COPD versus PBO+ICS/LABA. No additional safety concerns were identified with UMEC+ICS/LABA.

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COI Statement ARS, JR, AC, WAF, CQZ and YSP are employees of GSK and hold stocks/shares in GSK.

P125 TIOTROPIUM PLUS OLODATEROL COMBINATION THERAPY PROVIDES LUNG-FUNCTION BENEFITS WHEN COMPARED TO TIOTROPIUM ALONE, IRRESPECTIVE OF PRIOR TREATMENT WITH A LONG-ACTING BRONCHODILATOR: POST HOC ANALYSES OF TWO 1-YEAR STUDIES

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Rationale Tiotropium plus olodaterol (T+O) is a novel once-daily combination of the long-acting muscarinic antagonist (LAMA) tiotropium (T) and the recently approved long-acting β_2-agonist (LABA) olodaterol, for use as maintenance treatment in chronic obstructive pulmonary disease (COPD). These *post hoc* analyses of data from the two pivotal 1-year TONADO studies determined whether treatment with a long-acting

Abstract P125 Table 1

	No prior LABD treatment		Prior LABD treatment	
			All	
	T+O	T	T+O	T
Baseline characteristics				
n	426	454	603	579
Age (years), mean ± SD	62.7 ± 8.3	62.6 ± 8.8	64.6 ± 8.3	64.8 ± 8.2
Male, n (%)	291 (68.3)	338 (74.4)	442 (73.3)	417 (72.0)
Ex-smoker, n (%)	241 (56.6)	278 (61.2)	388 (64.3)	385 (66.5)
Post-bronchodilator FEV_1 (L), mean ± SD	1.38 ± 0.52	1.43 ± 0.54	1.32 (0.50)	1.32 (0.51)
Post-bronchodilator FEV_1 (% predicted), mean ± SD	50.7 ± 16.0	50.8 ± 15.7	48.3 ± 14.7	48.8 ± 15.6
Reversibility (mL), mean ± SD	158 ± 160	166 ± 144	169 ± 138	174 ± 147
Lung function after 24 weeks of treatment				
Adjusted mean FEV_1 AUC_{0-3}, (mL) ± SE	270 ± 1	154 ± 9	256 ± 8	150 ± 8
Adjusted mean trough FEV_1 (mL) ± SE	148 ± 1	72 ± 1	134 ± 8	86 ± 8
			GOLD 2	
	T+O	T	T+O	T
Baseline characteristics				
n	228	240	274	277
Age (years), mean ± SD	63.0 ± 8.2	62.5 ± 8.9	65.3 ± 8.9	64.8 ± 8.7
Male, n (%)	148 (64.9)	160 (66.7)	202 (73.7)	180 (65.0)
Ex-smoker, n (%)	117 (51.3)	128 (53.3)	176 (64.2)	179 (64.6)
Post-bronchodilator FEV_1 (L), mean ± SD	1.72 ± 0.44	1.77 (0.47)	1.69 (0.44)	1.69 (0.45)
Post-bronchodilator FEV_1 (% predicted), mean ± SD	63.2 ± 8.8	63.1 ± 8.4	62.0 ± 7.4	62.7 ± 8.1
Reversibility (mL), mean ± SD	175 ± 156	184 ± 163	201 ± 151	196 ± 170
Lung function after 24 weeks of treatment				
Adjusted mean FEV_1 AUC_{0-3}, (mL) ± SE	289 ± 13	175 ± 13	302 ± (12)	179 ± 12
Adjusted mean trough FEV_1 (mL) ± SE	146 ± 14	68 ± 14	156 ± 13	95 ± 13

SD, standard deviation; SE, standard error.

bronchodilator (LABD) prior to randomisation affected the lung-function benefits of T+O 5/5 μg (via Respimat®) compared to T 5 μg (via Respimat®).

Methods In the studies, 2124 patients had not received prior LABD treatment (T+O n = 426; T n = 454) and 3038 patients had (T+O n = 603, T n = 579; 60.6% LAMA, 78.8% LABA). Baseline characteristics for all patients and a sub-group with Global initiative for chronic Obstructive Lung Disease (GOLD) 2 lung-function impairment are presented in the Table 1. Forced expiratory volume in 1 s (FEV_1) area under the curve from 0–3 h ($AUC_{0–3}$) response (change from baseline) and trough FEV_1 response were primary end points in the studies.

Results Comparable responses for both FEV_1 $AUC_{0–3}$ and trough FEV_1 were observed in patients previously treated and untreated with LABD (see Table 1). The between-treatment differences (adjusted mean response [SE]; mL) for no prior LABD and prior LABD treatment, respectively, were: 116 (13) and 105 (11) for FEV_1 $AUC_{0–3}$, and 76 (14) and 49 (11) for trough FEV_1. In the GOLD 2 subgroup, the between-treatment differences (adjusted mean response [SE]; mL) for no prior LABD and prior LABD treatment, respectively, were: 114 (19) and 123 (17) for FEV_1 $AUC_{0–3}$, and 79 (20) and 61 (18) for trough FEV_1.

Conclusions Our analyses demonstrate the robust lung-function efficacy of T+O, compared to T alone, independent of the requirement for, or prior use of, LABD. These findings suggest a benefit of combination therapy over the mono-product as a first-line maintenance treatment.

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P126 EFFICACY OF ACLIDINIUM BROMIDE COMPARED WITH TIOTROPIUM AND PLACEBO IN SYMPTOMATIC PATIENTS WITH MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): POST-HOC ANALYSIS OF A PHASE IIIB STUDY

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Introduction and objective Maintaining bronchodilation and symptom control throughout the day and night is an important COPD therapeutic aim. Here, we compare 24-hour lung function and symptom control in symptomatic patients with moderate to severe COPD treated with aclidinium or tiotropium, two long-acting, muscarinic antagonists.

Methods This was a post-hoc analysis of a 6-week, double-blind, Phase IIIb study comparing aclidinium 400 μg BID with tiotropium bromide 18 μg QD or placebo in patients with moderate to severe COPD (NCT01462929). Symptomatic patients were defined as having an EXAcerbations of Chronic pulmonary disease Tool-Respiratory Symptoms (E-RS) baseline score ≥ 10 units. Primary endpoint: change from baseline in normalised FEV_1 AUC over 24-hours post-morning dose ($AUC_{–24/24h}$) at Week 6. Other endpoints: change from baseline in morning pre-dose (trough) FEV_1 and change from baseline in FEV_1 $AUC_{0–2/12h}$; $_{12–4/12h}$, E-RS, early-morning and night-time symptoms, and limitation of early-morning activities.

Results A total of 277/414 symptomatic patients were included; mean age was 62.1 years, 54.5% were current smokers, baseline FEV_1 1.41 ± 0.48 L. At Week 6, aclidinium 400 μg BID improved FEV_1 over 24 h from baseline vs placebo (Table 1). During the night-time period, aclidinium 400 μg BID improved FEV_1 from baseline vs tiotropium 18 μg QD. At Week 6, improvements in trough FEV_1 from baseline were observed with aclidinium vs tiotropium and placebo. Aclidinium improved E-RS total score from baseline vs tiotropium and placebo. Moreover, aclidinium improved early-morning and night-time symptom severity from baseline vs tiotropium and placebo over the treatment period (see Table 1 for all results described above). Limitation of early-morning activities caused by COPD symptoms was also improved with aclidinium vs tiotropium and placebo ($p < 0.05$). Tolerability has been previously reported (Beier COPD 2013) where adverse events (AEs) were similar in each arm, few anticholinergic AEs or serious AEs occurred in any group, and aclidinium was well tolerated.

Conclusions Aclidinium 400 μg BID improved bronchodilation, particularly during the night-time period, as well as early morning, daily and night-time symptoms, and early-morning limitation of activity in symptomatic patients compared with either tiotropium 18 μg QD or placebo.

Abstract P126 Table 1 Spirometric and symptomatic variables in symptomatic patients with COPD (baseline E-RS ≥10)

	Day 1			Week 6		
Change from baseline in normalised FEV_1 vs placebo, mL	**Aclidinium 400 μg**	**Tiotropium 18 μg**	**Aclidinium vs tiotropium**	**Aclidinium 400 μg**	**Tiotropium 18 μg**	**Aclidinium vs tiotropium**
FEV_1 $AUC_{–24/24h}$	150*	87*	63†	140**	106*	34
FEV_1 $AUC_{12–24/12h}$ (night-time)	157**	67*	90†	153**	90**	63†
FEV_1 $AUC_{–12}$ (day time)	147**	112**	35	126*	123*	3
Morning pre-dose (trough) FEV_1	136**	68*	68†	137*	70*	65†
E-RS Total Score over 6 weeks	-	-	-	-2.15*	-0.98	-1.17†
[a]Early morning symptom severity over 6 weeks	-	-	-	-0.25*	-0.11	-0.14†
(% reduction)				(-9.54%)	(-4.33%)	(-5.21%)
[b]Night-time symptom severity over 6 weeks	-	-	-	-0.23*	-0.09	*-0.14*†
(% reduction)				(-10.31%)	(-4.23%)	(-6.09%)

*p < 0.05 vs placebo; **p ≤ 0.0001 vs placebo; †p < 0.05 vs tiotropium.
[a]Least squares mean change from baseline in the severity of early morning symptoms over 6 weeks: 1 = No symptoms, 2 = Mild, 3 = Moderate, 4 = Severe, 5 = Very severe.
[b]Change from baseline in the severity of night-time symptoms over 6 weeks: 1 = No symptoms, 2 = Mild, 3 = Moderate, 4 = Severe, 5 = Very severe.
AUC, area under the curve; COPD, chronic obstructive pulmonary disease; E-RS, EXAcerbations of Chronic pulmonary disease Tool-Respiratory Symptoms; FEV_1, forced expiratory volume in 1 s.